In the Specification

Please amend paragraphs **[0161], [0162], [0167], [0169],** and **[0174]** of the Specification as follows:

[0161] ~~**RT± PCR**~~ **RT-PCR** The exon 5 (sense primer 5'-GAC TGT ATG GAT GTTCTG TCA G-3'; SEQ ID NO:65) and exon 6 (antisense primer 5'-ATT TGTCCT GGC AGA CGA AGC A-3'; SEQ ID NO:66) were designed on the basis of published RAR ß2 transcript (de The' et al., 1990;van der Leede et al., 1992) and used to amplify 50 ng of DNase treated total RNA using the Superscript One-StepRT± PCR System (Life Technologies). RT± PCR with actin primers (sense primer 5'-ACC ATG GAT GAT GAT ATCG-3'; SEQ ID NO:67 and antisense primer 5'-ACA TGG CTG GGG TGTTGA AG-3'; SEQ ID NO:68) was used as an internal RNA control.

[0167] **The RAR β2 promoter is methylated in breast cancer cell lines independently of their ER status and RA-inducibility** RAR transcription was first tested in a panel of breast cancer cell lines grown in the absence of exogenous RA, by reverse transcriptase-PCR (RT ± PCR), using primers encompassing exons 5 and 6 (de The' et al.,1990; van der Leede et al., 1992; Toulouse et al., 1997). Under these conditions, only one cell line, Hs578t,produced a detectable 256 bp ~~RT± PCR~~ RT-PCR product. Thus, previous reports were confirmed that RAR β gene expression is down regulated/lost in breast cancer cell lines. Growing cells in the presence of RA can assess the distinction between down regulation and loss. As previously reported (Swisshelm et al., 1994; Liu et al., 1997; Shang et al., 1999), we observed induction of RAR ß expression and growth inhibition inT47D, MDA-MB-435, MCF7 and ZR75-1 cell lines treated for 48 h with 1 μM RA, but not in the MDA-MB-231 and MDA-MB-468 cell lines.

[0169] The HDAC inhibitor TSA can reactivate RAR β expression in RA-resistant cells; demethylation of the RAR ß2 promoter is not an absolute requirement for RAR ß reactivation The chromatin status at a given locus can be dynamically influenced by the degree of acetylation/deacetylation due to HAT/HDAC activities. Absence of RAR ß regulatory factors, like RAR a, as well as DNA-methylation, can contribute to pattern chromatin modifications at RAR ß promoter in RA-resistant cell lines. One of these cell lines, MDA-MB-231, lacks RA-inducible RARα activity (Shao et al., 1994) and displays a RAR ß2 methylated promoter. A subsequent study was designed to probe indirectly whether the level of HDAC at RAR ß2 can influence RAR ß expression, by testing the effect of TSA, a HDAC inhibitor on MDA-MB-231cells (Yoshida et al., 1995). Cells were treated for 2 days, in the presence or absence of 100 ng/ml TSA alone, or in combination, with 1 μM RA. By using ~~RT± PCR~~ RT-PCR, it was clear that, unlike cells treated with RA alone, cells treated with a combination of RA and TSA re-expressed RAR ß mRNA. Under the same experimental conditions, 100 ng/ml TSA alone, or in combination with 1 mM RA, produced 77and 92% growth inhibition, respectively. Treatment with 1μM RA alone did not affect significantly growth inhibition (52%). By MSP analysis, it was assessed that RAR ß expression was restored in the presence of a methylated RAR ß2 promoter. This finding indirectly shows that global alterations of HDAC activity, generated by TSA in MDA-MB-231 cells, involved RAR ß2 resulting in RA-induced RAR ß expression. Further, demethylation at RAR ß2 did not seem to be an absolute requirement for RAR ß gene expression inMDA-MB-231 cells. Noteworthy, persistence of methylation at RAR ß2 was observed also in MCF7 cells where RAR ß transcription could be restored in the presence of RA. Growth inhibition was observed in cells treated with TSA alone, or in combination, with RA. Very likely, RAR ß along with TSA, a drug known to induce growth inhibition(Yoshida *et al.*, 1995), contributed to the massive growth inhibitory effect that was observed.

[0174] Methylation specific PCR (MSP) and sodium bisulfite DNA sequencing One μg of genomic DNA was treated with sodium bisulfite[21] and was analyzed for MSP using primer sets specific for methylated DNA: 5'-TTTAGCGGTGGCGTTCG-3' (sense; SEQ ID NO:69) and 5'-ATACGACTTCGAATCACGTA-3' (antisense; SEQ ID NO:70), and primers specific for unmethylated DNA: 5'-TTGGTTGGAAGTTGGGTG-3' (sense; SEQ ID NO:71), and 5'-AATACAACTTCAAATCACATAC-3'(antisense; SEQ ID NO:72) which yielded products of 183 and 213 bp respectively. Sodium bisulfite treated DNA was used to PCR-amplify the HOXA5 promoter region –97 to –303 bp, using the primers 5'-ATTTTGTTATAATGGGTTGTAAT-3' (sense; SEQ ID NO:73) and 5'-AACATATACTTAATTCCCTCC-3' (antisense; SEQ ID NO:74). The product was purified using a Qiagen PCR purification kit (Qiagen Corp.) and was sequenced using the sense primer with an ABI automated fluorescent sequencer according to the manufacturer's instructions.